20

REMARKS

The Office Action, Applicant's Response to Restriction Requirement Amendment

The Examiner required restriction, under 35 U.S.C. § 121, and required Applicant to elect a single invention to which the claims must be restricted. The Examiner designated the following three claim groups:

1. Group I: Claims 1-7, 9-23, 42, 43, 46, and 47, drawn to a method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell involving delivering to the cell a PTTG carboxy-terminal-related polynucleotide complexed with a cellular uptake agent;

2. Group II: Claim 8, drawn to a method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian cell, wherein the polynucleotide is an antisense oligonucleotide complexed with a cellular uptake agent;

3. Group III: Claims 24-41, 44, 45, 48, and 49, drawn to a method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian cell involving delivering to the cell a PTTG carboxy terminal peptide, or a functional fragment thereof complexed with a cellular uptake agent.

In response to the restriction requirement, Applicant elects **Group** II, without traverse. Applicant requests the Examiner to cancel Claims 8, 24-41, 44, 45, 48, and 49, without prejudice as belonging to non-elected claim groups. A further

election of rat, murine or human PTTG carboxy-terminal-related polynucleotides or PTTG-C peptides was also required. In response, Applicant elects **human** PTTG carboxy-terminal-related sequences (SEQ ID NO:9 and SEQ ID NO:10). Applicant's elections are made with a complete reservation of all rights under 35 U.S.C. § 121.

The amendments in the specification at page 67, lines 6, 7, and 8 are to correct obvious typographical errors.

In addition, Applicant has amended Claims 1, 9, 14, 15, 46, and 47 to recite the elected SEQ ID NOs:9 and/or 10, and to delete the recitations of non-elected SEQ. ID. NOS.: 16, 17, 18 and/or 19, which amendments are without prejudice. In Claims 1, 14, and 15, periods have been removed from the term "SEQ ID NO".

The amendment of Claim 1 is for greater clarity and is supported, e.g., in Claims 11-13 as originally filed; and in the specification, e.g., at page 35, lines 17-25; and at page 36, lines 20-24. Claims 11-13 are made redundant by the amendment of Claim 1 and are therefore canceled, without prejudice.

The amendment to Claim 9 is for greater clarity and is supported in the specification, e.g., at page 15, lines 6-12.

The deletion of the phrase "any of" in element (B) of Claim 14 is made necessary in order to conform to standard English usage concerning the singular.

In Claim 14, the cancellation of Claim 12 makes necessary the change of dependency from Claim 1 instead of Claim 12. In Claim 14, the insertion of a semicolon at the end of element (A) is merely to correct an obvious typographical error. The amendment of step D in Claim 14, is supported, e.g., by Claim 16 as originally filed; and in the specification, e.g., at page 35, lines 17-25; and at page 36, lines 20-24.

In Claim 15, the recitation of "proline-rich region of SEQ ID NO:9" is supported, e.g., by Claim 16 as originally filed; and in the specification, e.g., at page 35, lines 17-25; and at page 36, lines 20-24.

Claim 16 is made redundant by the amendments to Claim 14-15, and is therefore canceled, without prejudice.

The amendments to Claims 46 and 47, deleting the word "essentially" are for greater clarity.

Respectfully submitted,

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Version with Markings To Show Changes Made

In the Specification:

At page 67, lines 5-9, please delete the paragraph and insert therefor the following paragraph:

--Control and h*PTTG*-transfected cells were tested for anchorage-independent growth in soft agar;[.] 3 ml of soft agar (20% of 2X DMEM, 50% DMEM, 10% fetal bovine serum, and 20% of 2.5% agar, melted and mixed at 45°C) were added to 35-mm tissue dishes. 10,000 cells were mixed with 1 ml soft agar and added to each dish, and [i]incubated for 2 weeks until colonies could be counted and photographed.--.

In the Claims:

Please cancel Claims 8, 24-41, 44, 45, 48, and 49, without prejudice, as being directed to a non-elected claim group. Further, please cancel Claims 11-13, and 16, without prejudice. Please amend Claims 1, 9, 14, 15, 46, and 47 as follows.

1.(Amended) A method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell, comprising:

delivering to a mammalian breast or ovarian cell that overexpresses *PTTG*, a composition comprising a PTTG carboxy-terminal-related polynucleotide, said polynucleotide encoding a PTTG-C peptide selected from the group consisting of

(A) peptides having an amino acid sequence consisting of SEQ ID NO:9; and

(B) peptide fragments of (A) that comprise at least 15 contiguous amino acid residues, including a proline-rich region of SEQ ID NO:9, and that function to downregulate endogenous PTTG expression and/or PTTG function;

said polynucleotide being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to allow the polynucleotide to enter the cell, whereby neoplastic cellular proliferation and/or transformation of the cell is inhibited.

2.(Reiterated) The method of Claim 1, wherein the cell is of human origin.

3.(Reiterated) The method of Claim 1, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.

4.(Reiterated) The method of Claim 1, wherein the cell is a malignant cell.

5.(Reiterated) The method of Claim 1, wherein the composition is delivered to the cell in vitro.

6.(Reiterated) The method of Claim 1, further comprising administering the composition to a mammalian subject, such that the composition is delivered to the cell in vivo.

7.(Reiterated) The method of Claim 1, wherein the polynucleotide is a DNA or DNA analog.

Claim 8 is canceled.

9.(Amended) The method of Claim 1, wherein the polynucleotide is a [protein] peptide nucleic acid.

10.(Reiterated) The method of Claim 7, wherein the composition further comprises an expression vector comprising a promoter, and the PTTG carboxy-terminal-related polynucleotide is operatively linked to the promoter in a transcriptional unit.

Claims 11-13 are canceled.

14.(Amended) The method of Claim 1[2], wherein the polynucleotide has a nucleotide sequence consisting of

(A) (SEQ[.] ID[.] NO[.]:10)[, (SEQ. ID. NO.:18), or (SEQ. ID. NO.:19)];

(B) a degenerate coding sequence of [any of] (A);

(C) a sequence complementary to any of (A) or (B); or

(D) a polynucleotide fragment comprising at least 45 contiguous nucleotides of any of (A), (B) or (C) that comprises contiguous nucleotide positions 49-81 of SEQ ID NO:10 or a degenerate sequence.

15.(Amended) A method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell comprising:

delivering to a mammalian breast or ovarian cell that overexpresses PTTG, a composition comprising an expression vector comprising a promoter and a polynucleotide, said polynucleotide comprising a first DNA segment encoding a mammalian PTTG-C peptide, said polynucleotide being operatively linked to the promoter in a transcriptional unit, said PTTG-C peptide being selected from the group consisting of

(A) peptides having an amino acid sequence consisting of (SEQ[.] ID[.] NO[.]:9)[, (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17)];

[(B) mammalian PTTG-C peptides having at least about 60% sequence homology with (A);] and

([C]B) peptide fragments of (A) [or (B)] that comprise at least 15 contiguous amino acid residues, including a proline-rich region of SEQ ID NO:9, and that function to downregulate endogenous *PTTG* expression and/or PTTG function, said expression vector being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the cell, such that the PTTG-C peptide is expressed in the cell, whereby

neoplastic cellular proliferation and/or transformation of the cell is inhibited.

Claim 16 is canceled.

17.(Reiterated) The method of Claim 15, wherein the polynucleotide further comprises a second DNA segment encoding an uptake-enhancing and/or importation-competent peptide segment.

18.(Reiterated) The method of Claim 17, wherein the cellular uptake-enhancing and/or importation-competent polypeptide is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

19.(Reiterated) The method of Claim 15, wherein the cell is of human origin.

20.(Reiterated) The method of Claim 15, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.

21.(Reiterated) The method of Claim 15, wherein the cell is a malignant cell.

22.(Reiterated) The method of Claim 15, wherein the composition is delivered to the cell in vitro.

23.(Reiterated) The method of Claim 15, further comprising administering the composition to a mammalian subject in need of treatment, such that the expression vector is delivered to the cell in vivo.

Claims 24-41 are canceled.

42.(Reiterated) The method of Claim 1, further comprising administering a cytotoxic chemotherapeutic agent to the cell simultaneously with or after delivering to the mammalian breast or ovarian the composition comprising the PTTG carboxy-terminal-related polynucleotide.

43.(Reiterated) The method of Claim 15, further comprising administering a cytotoxic chemotherapeutic agent to the cell simultaneously with or after delivering to the breast or ovarian cell the composition comprising the expression vector.

Claims 44-45 are canceled.

46.(Amended) The method of Claim 42, wherein the cytotoxic chemotherapeutic agent is selected from the group [essentially] consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

47.(Amended) The method of Claim 43, wherein the cytotoxic chemotherapeutic agent is selected from the group [essentially] consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

Claims 48-49 are canceled.